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PATENT APPLICATION

ATTORNEY DOCKET NO. 10991394-5

IN THE
UNITED STATES PATENT AND TRADEMARK OFFICE

Inventor(s): Michel G.M. Perbost

Serial No.: 09/895,050 **Examiner:** Arun K. Chakrabarti

Filing Date: 06/29/2001 **Group Art Unit:** 1634

Title: BIOPOLYMER ARRAYS AND THEIR FABRICATION

ASSISTANT COMMISSIONER FOR PATENTS
Washington, D.C. 20231

TRANSMITTAL OF APPEAL BRIEF

Sir:

Transmitted herewith in triplicate is the Appeal Brief in this application with respect to the Notice of Appeal filed on **11/18/2002**.

The fee for filing this Appeal Brief is (37 CFR 1.17(c)) $320.00.

(complete (a) or (b) as applicable)

The proceedings herein are for a patent application and the provisions of 37 CFR 1.136(a) apply.

(X) (a) Applicant petitions for an extension of time under 37 CFR 1.136 (fees: 37 CFR 1.17(a)-(d) for the total number of months checked below:

( )	one month	$110.00
(X)	two months	$410.00
( )	three months	$930.00
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( ) The extension fee has already been filled in this application.

( ) (b) Applicant believes that no extension of term is required. However, this conditional petition is being made to provide for the possibility that applicant has inadvertently overlooked the need for a petition and fee for extension of time.

Please charge to Deposit Account 50-1078 the sum of **$730.00**. At any time during the pendency of this application, please charge any fees required or credit any overpayment to Deposit Account 50-1078 pursuant to 37 CFR 1.25.

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Typed Name: **Elizabeth Miller**

Signature: Elizabeth Miller

Respectfully submitted,

Michel G.M. Perbost

By _____

Gordon M. Stewart
Attorney/Agent for Applicant(s)
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Date: **03/17/2003**

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Agilent Docket No. 10991394-5

In the United States Patent and Trademark Office
Board of Patent Appeals and Interferences

In re Application of

Inventor: Perbost

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Examiner: Arun K. Chakrabarti

I hereby certify that this correspondence is being deposited today with the United States Postal Service as first class mail in an envelope addressed to Assistant Commissioner for Patents, Washington, D.C. 20231.

Elizabeth Miller
Elizabeth Miller
March 17, 2003
Date

Hon. Assistant Commissioner for Patents
BOX: BOARD OF PATENT APPEALS AND INTERFERENCES
Washington, D.C. 20231

Sir:

APPEAL BRIEF

A Notice of Appeal was mailed Nov. 18, 2002. A request for a 2-month extension to file the present Appeal Brief is enclosed.

Respectfully submitted,

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APPEAL BRIEF

I. Real Party in Interest

The real party in interest is Agilent Technologies, Inc., assignee of the present application and invention.

II. Related Appeals and Interferences

There are no other related appeals or interferences.

III. Status of Claims

Claims 29-35 are pending. Claim 31 is allowed. Claims 29, 30, 32-35 stand rejected and are the subject of the present appeal. The only independent claims are as follows (claims directly or indirectly dependent on each are indicated in parentheses after each): **29** (30, 34, 35); **31**; **32** (33).

IV. Status of Amendments

The last amendments made to the present application were in the before final Amendment and Response mailed June 13, 2002. No Advisory Action has been received in reply to the after final Response (argument only, no amendment) mailed Nov. 18, 2002. All the pending claims stand as amended in the June 13, 2002 Amendment and Response and are reproduced in the attached APPENDIX.

V. Summary of the Invention

The following provides an explanation of the invention of the claims, with reference to exemplified embodiments disclosed in the specification and drawings.

The present invention provides in independent claim 29 an apparatus for fabricating an addressable array of biopolymers on a substrate (FIGS. 1-3, page 9, lines 6-17) according to a target pattern. The apparatus includes a deposition system (page 11, lines 17-18; FIG. 6) which can separately dispense onto a substrate: drops of fluid compositions of different biomonomers (page 9, lines 31-32; page 7, line 21 to page 8, line 11), each biomonomer with a first linking group which must be activated for linking to a substrate bound moiety; and dispense a fluid composition of a solid activator (page 9, lines 26-28; page 15, lines 18-25).

A processor (FIG. 6, 140) operates the deposition system. The processor derives from a target array pattern a target drive pattern for operating the deposition system to form the array (page 13, lines 11-26). This target drive pattern includes instructions to the deposition system to perform the following at each of multiple regions at which a biomonomer is to be deposited (page 14, lines 5-17):

(i) deposit the fluid composition of solid activator separate from and preceding deposition of the biomonomer;

(ii) allow sufficient time for evaporation to leave solid activator at the region; and

(iii) then deposit the biomonomer.

The present invention recognizes that deposited drops of biomonomers (such as phosphoramidites), once activated by the activator, may undesirably react at their surface with components in the ambient atmosphere (such as water vapor). This can lead to lowered concentration of phosphoramidite available for linking to the substrate surface and hence lowered concentration of probe linked to the surface (page 2, lines 16-29). However, by forming the solid activator in (ii) above as a result of evaporation and before depositing the biomonomer in (iii), causes activated biomonomer to be present at highest concentration adjacent the substrate surface and away from the drop surface (where it could undesirably react with atmosphere components such as water vapor). This allows time for the activated biomoner to link to the surface before it has the chance to undesirably react with the atmosphere component (such as water vapor). The foregoing is explained on page 10, lines 14-21 in connection with FIG. 5.

The invention may also be a computer program product (claim 32) carrying a computer program which, when loaded into a computer derives a target drive pattern including instructions for the deposition system to perform items (i) through (iii) of clam 29. The instructions may include (in claim 33) depositing sufficient biomonomer fluid composition at a region (FIG. 4, #44) which will cover an area greater than that covered by a preceding droplet (FIG. 4, #40) of activator fluid composition at the same region (page 10, lines 1-7). Note that this leaves the peripheral edges of the solidified activator (FIG. 5, #42), and hence resulting activated biomonomer, away from the outside edges of the deposited drop #44 where it might otherwise undesirably react with moisture or the like in the ambient atmosphere.

VI. Issues

The outstanding rejection is summarized in the final Action mailed July 16, 2002 as follows:

> Are claims 29, 30, 32-35 unpatentable under 35 U.S.C. 103(a) over Baldeschwieler et al. (WO 95/25116) in view of Hirschbein et al. (US 5,859,233)?

VII. Grouping of Claims

For the reasons discussed in Section VIII below, the claims are grouped as listed below. Claims within each group for a rejection are considered to stand or fall together for the purposes of that rejection. Additional reasons for reversal in connection with Group II are provided below.

Group I - Claims 29, 30, 32, 34, 35
Group II – Claim 33

VIII. Argument

First, with regard to this (and other) rejections, the Examiner bears the initial burden of establishing a *prima facie* of rejection. This has been made clear by the Federal Circuit in , for example, *In re Oetiker* 24 USPQ2d 1443 @ 1444 (Fed. Cir.; 1992):

> "As discussed in *In re Piasecki* , the examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a prima facie case of unpatentability. If that burden is met, the burden of coming forward with evidence or argument shifts to the applicant."

Further, in order for the Examiner to establish a *prima facie* case of obviousness, the prior art must provide the requisite suggestion or motivation, not the Examiner based on a hindsight reconstruction using the Applicants' specification. This has been clearly stated by the Federal Circuit in, for example, In re Vaeck 20 USPQ2d 1438 (1991) @ 1442:

> "Where subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under s. 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. See *In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. *Id.*"

Rejection of Claims of Groups I and II (Claims 29, 20, 32-35)

Claims 29, 30 and 32-35 were rejected under 35 U.S.C. 103(a) over Baldeschwieler et al. (WO 95/25116) in view of Hirschbein et al. (US 5,859,233). All of the rejected claims 29, 30, 32-35 require the following:

> (i) deposit the fluid composition of solid activator separate from and preceding deposition of the biomonomer;

(ii) allow sufficient time for evaporation to leave solid activator at the region; and

(iii) then deposit the biomonomer.

The Examiner contended that all these elements can be found in Baldeschwieler et al. with the exception that Baldeschwieler et al. do not teach an apparatus where sufficient time is allowed for evaporation to leave solid activator at the region then depositing the biomonomer. The Examiner then contended that this latter feature is found in Hirschbein et al. and that it would have been obvious to use such a feature in Baldeschwieler et al. thereby leading to the claimed invention.

However, this rejection is respectfully traversed on the basis that the Examiner miss-reads Hirschbein et al., and that it does not in fact teach or suggest allowing sufficient time for evaporation to leave a solid activator in a region to which is then applied a biomonomer, as required by the rejected claims.

Before looking at the portions of Hirschbein et al. specifically relied upon by the Examiner, it is believed that they are misinterpreted by the Examiner due to the use of the word "dry" in that patent. In particular, Hirschbein et al. makes it clear that "dry" is used in the sense of no water being present, not that a solid form of the activator is somehow present. See in particular, column 12, lines 35-39:

> "A great amount of care should be exercised to use **very dry (free from water)** monomer, activator, and solvent for the coupling step and for the solvent used to wash the solid support immediately before the coupling step. (emphasis added)

Turning now to the particular portions of Hirschbein et al. relied on by the Examiner, the Examiner first references (page 4, 2nd paragraph of the Final Rejection) in Hirschbein et al. Example 2 and column 12, lines 27-39, and column 13, line 46 to column 14, line 9, for the concept of allowing sufficient time for evaporation to leave a solid activator. Example 2 though, deals only with preparation of one of the phosphoramidite monomers (see line 20, 3-4 "Preparation of 2'-Deoxy -3'-tritylaminocytidine-5'-phosphoramidite Monomers") using Scheme III of column 24-25, and not with linking multiple monomers as done later in the Hirschbein et al. patent or in

Baldeschwieler et al. Accordingly, this does not provide any teaching as to how to use Hirschbein et al.'s monomer coupling activator (note that Hirschbein et al.'s usual tetrazole class of activators described in column 12, lines 26-39, is not even present in Example 2).

The Examiner next references column 13, line 46 to column 14, line 4 for the benefits of using "dry reagents and solvents". As pointed out above, **Hirschbein et al. specifically defines "dry" not as being in a solid form (as required by the rejected claims) but simply as being free of water**. Thus, there is no teaching here as to allowing sufficient time for evaporation to leave a solid activator, as required by all the rejected claims, but merely a teaching of the benefits of using reagents which are free from water.

Thus, while Hirschbein et al. does in fact teach using "dry reagents", this only means reagents without water and the relied upon portions of Hirschbein et al. therefore do not teach what the Examiner alleges (i.e. allowing sufficient time for evaporation to leave a solid activator, as required by the rejected claims). Furthermore, a look at Hirschbein et al.'s actual coupling reactions (Examples 10-15, 19, and 23) make it clear that he simply uses a dry solution (free of water) of tetrazole activator for their coupling reactions. Specifically the tetrazole activator solvent is acetonitrile; see column 32, line 16 for Example 10, the same solution being used in Examples 11-13 and 15; column 34, lines 57-58 for Example 14 with the same solution used again in Example 23; and column 44, line 34 for Example 19. None of those Examples (nor anything the Examiner has cited) suggest for some unexplained reason allowing sufficient time for the "dry" (i.e. free from water) solvent to evaporate to leave a solid activator.

Thus, while the Examiner correctly points out that Hirschbein et al. refers to using a dry solvent (i.e. free of water) for the activator, he has not pointed to anything in Hirschbein et al. where this dry solvent is allowed sufficient time to evaporate to leave a solid activator before a biomonomer is then applied. Accordingly, the Examiner has failed in his burden of establishing a *prima facie* case of obviousness by pointing to the required suggestion or motivation for the claimed apparatus (or computer program product) in the prior art.

For the above reasons, it is respectfully submitted that the rejection of claims 29, 30 and 32-35 should be reversed and those claims allowed in addition to allowed claim 31.

Additional Arguments with Respect to Claim 33

Claim 33 is dependent upon claim 32 and additionally requires:

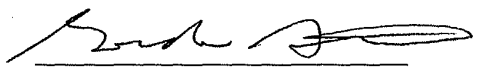
> instructions to the deposition system to deposit sufficient biomonomer fluid composition at a region which will cover an area greater than that covered by a preceding droplet of activator fluid composition at the same region" (emphasis added)

In the Final Rejection the Examiner does not even allege that such a feature is disclosed or suggested in the cited references. Accordingly, the Examiner has failed in his burden to establish a *prima facie* case of obviousness of claim 33.

For this additional reason the rejection of claim 33 should be reversed.

Accordingly, for the reasons discussed above, the rejection of claims 29, 30, 32-35 should be reversed.

Respectfully submitted,



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APPENDIX – Claims

29. (REJECTED) An apparatus for fabricating an addressable array of biopolymers on a substrate according to a target pattern, comprising:

(a) a deposition system which can separately dispense onto a substrate, fluid compositions of different biomonomers each with a first linking group which must be activated for linking to a substrate bound moiety, and a fluid composition of a solid activator;

(b) a processor to operate the deposition system, which processor derives from the target array pattern a target drive pattern for operating the deposition system to form the array, the target drive pattern comprising instructions to the deposition system to perform the following at each of multiple regions at which a biomonomer is to be deposited:

(i) deposit the fluid composition of solid activator separate from and preceding deposition of the biomonomer;

(ii) allow sufficient time for evaporation to leave solid activator at the region; and

(iii) then deposit the biomonomer.

30. (REJECTED) An apparatus according to claim 29 wherein the deposition system comprises multiple pulse jets which can dispense droplets of the different biomonomer fluid compositions and at least one pulse jet which can separately dispense the activator fluid composition, each jet comprising: a chamber with an orifice; and an ejector which, when activated, causes a droplet to be ejected from the orifice.

31. (ALLOWED) An apparatus for fabricating an addressable array of biopolymers on a substrate according to a target pattern, comprising:

(a) a deposition system which can separately dispense onto a substrate, fluid compositions of different biomonomers each with a first linking group which must be

activated for linking to a substrate bound moiety, and a fluid composition of a solid activator; and

(b) a processor to operate the deposition system, which processor derives from the target array pattern a target drive pattern for operating the deposition system to form the array, the target drive pattern comprising instructions to the deposition system to deposit the fluid composition of solid activator at each region at which a biomonomer is to be deposited, separate from and preceding deposition of the biomonomer;

wherein the deposition system comprises multiple pulse jets which can dispense droplets of the different biomonomer fluid compositions and at least one pulse jet which can separately dispense the activator fluid composition, each jet comprising: a chamber with an orifice; and an ejector which, when activated, causes a droplet to be ejected from the orifice; and

wherein the target drive pattern comprises ejector instructions such that a droplet of biomonomer fluid composition deposited at a region will cover an area greater than that covered by a preceding droplet of activator fluid composition at the same region.

32. (REJECTED) A computer program product, for use on an apparatus for fabricating an addressable array of biopolymer probes on a substrate according to a target array pattern, the program product comprising: a computer readable storage medium having a computer program stored thereon which, when loaded into a computer of the apparatus performs the steps of:

deriving from the target array pattern a target drive pattern for operating a deposition system of the apparatus to form the array, the target drive pattern comprising instructions to the deposition system to perform the following at each of multiple regions at which a biomonomer is to be deposited:

(i) deposit the fluid composition of solid activator separate from and preceding deposition of the biomonomer;

(ii) allow sufficient time for evaporation to leave solid activator at the region; and

(iii) then deposit the biomonomer.

33. (REJECTED) A computer program product according to claim 32 wherein the target drive pattern comprises instructions to the deposition system to deposit sufficient biomonomer fluid composition at a region which will cover an area greater than that covered by a preceding droplet of activator fluid composition at the same region.

34. (REJECTED) An apparatus according to claim 29 wherein the processor derives a target drive pattern which repeats (i) to (iii) at each of multiple features.

35. (REJECTED) An apparatus according to claim 29 wherein the deposition system comprises a head having multiple pulse jets which can dispense droplets of the different biomonomer fluid compositions.